(FILE 'HOME' ENTERED AT 08:59:20 ON 29 JUL 2002)

FILE 'BIOSIS, MEDLINE, INPADOC' ENTERED AT 08:59:28 ON 29 JUL 2002

FILE 'BIOSIS, MEDLINE, INPADOC, CAPLUS' ENTERED AT 08:59:34 ON 29 JUL 2002

```
L1            69 URINE AND TH1
L2            44 DUPLICATE REMOVE L1 (25 DUPLICATES REMOVED)
L3            46 URINE AND TH2
L4            31 DUPLICATE REMOVE L3 (15 DUPLICATES REMOVED)
L5             7 L4 NOT L2
L6            23 HCG AND (TH1 OR TH2)
L7            13 DUPLICATE REMOVE L6 (10 DUPLICATES REMOVED)
L8            41 CHORIONIC AND (TH1 OR TH2)
L9            24 DUPLICATE REMOVE L8 (17 DUPLICATES REMOVED)
L10           21 L9 NOT L2
L11           20 L10 NOT L4
L12           13 L11 NOT L7

=>
```

L2 ANSWER 6 OF 44 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3

AN 2002:77491 BIOSIS

DN PREV200200077491

TI Inhibition of diabetes in NOD mice by human pregnancy factor.

AU Khan, Nisar A. (1); Khan, Afshan; Savelkoul, Huub F. J.; Benner, Robbert

CS (1) Department of Immunology, Erasmus University and University Hospital Rotterdam, 3000 DR, Rotterdam Netherlands

SO Human Immunology, (December, 2001) Vol. 62, No. 12, pp. 1315-1323. print. ISSN: 0198-8859.

DT Article

LA English

AB Clinical symptoms of **Th1** mediated autoimmune diseases regress in many patients during pregnancy. A prominent feature of pregnancy is the presence of human chorionic gonadotrophin hormone (hCG) in blood and **urine**. In this report we tested the effect of clinical grade hCG (c-hCG) on the development of diabetes, a **Th1** mediated autoimmune disease, in nonobese diabetic (NOD) mice. We show that treatment of NOD mice with c-hCG before the onset of clinical symptoms lowered the increased blood glucose levels, reversed the established inflammatory infiltrate of pancreatic tissue, and profoundly inhibited the development of diabetes for prolonged time. c-hCG also induced profound inhibition of the functional activity (i.e. production of IFN-gamma) of **Th1** cells. Transfer of spleen cells from c-hCG-treated NOD mice into immunocompromised NOD.SCID mice inhibited the development of diabetes in these otherwise non-treated mice. This shows that the treatment of the donor NOD mice induced persistent changes in the immune system. The antidiabetic activity of c-hCG was not caused by heterodimeric hCG or its subunits. Instead, this antidiabetic activity resided in a fraction of c-hCG preparation that contains a 400-2000 Dalton natural (immuno) modulatory pregnancy factor (NMPF).

L2 ANSWER 4 OF 44 CAPLUS COPYRIGHT 2002 ACS
AN 2001:729773 CAPLUS
DN 135:283540
TI Fragments of human chorionic gonadotropin (HCG) as immunoregulator
IN Khan, Nisar Ahmed; Benner, Robbert
PA Erasmus Universiteit Rotterdam, Neth.
SO Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1138692	A1	20011004	EP 2000-201139	20000329
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2001072831	A2	20011004	WO 2001-NL259	20010329
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	EP 2000-201139	A	20000329		

AB The invention relates to the field of immunol., more specifically to the field of immune-mediated disorders such as allergies, auto-immune disease, transplantation-related disease or inflammatory disease. The invention provides among others an immunoregulator (NMPF), use of an NMPF in prepg. a pharmaceutical compn. for treating an immune-mediated disorder, a pharmaceutical compn. and a method for treating an immune-mediated disorder. A method is also claimed for diagnosing a pregnancy related immune-mediated disorder such as preeclampsia comprising detg. in a sample, preferably a **urine** sample, the relative ratio of a relative long-chain peptide vs. a relative short-chain peptide, said peptides derivable from breakdown of beta-HCG.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

2

AN 2002:149271 BIOSIS

DN PREV200200149271

TI Inhibition of septic shock in mice by an oligopeptide from the beta-chain of human chorionic gonadotrophin hormone.

AU Khan, Nisar A. (1); Khan, Afshan; Savelkoul, Huub F. J.; Benner, Robbert

CS (1) Department of Immunology, Erasmus University and University Hospital Rotterdam, 3000 DR, Rotterdam: khan@immu.fgg.eur.nl Netherlands

SO Human Immunology, (January, 2002) Vol. 63, No. 1, pp. 1-7. print. ISSN: 0198-8859.

DT Article

LA English

AB Human chorionic gonadotrophin (hCG) is a heterodimeric placental glycoprotein hormone required in pregnancy. In human pregnancy **urine** and in commercial hCG preparations (c-hCG) it occurs in a variety of forms, including breakdown products. Several reports have suggested modulation of the immune system by intact hormone, but such effects of breakdown products have not been reported. In a related article (Hum Immunol 62:1315, 2001), it is reported that a 400-2000 Dalton (Da) fraction from c-hCG and from human pregnancy **urine** inhibits **Th1**-mediated diabetes in NOD mice. The active component(s) were called natural (immuno)modulatory pregnancy factor(s) (NMPF). This study reports that a single treatment with the same low molecular weight NMPF fraction up to 24-h after high dose lipopolysaccharide (LPS) injection inhibited septic shock in mice. This counteracting effect of NMPF paralleled the downregulation of the effects of LPS on the production of macrophage migration inhibitory factor (MIF) by spleen cells, on the plasma level of liver amino-transferase, and on the expression of several splenic lymphocyte and macrophage surface markers. Based on the primary structure of the beta-chain of hCG a synthetic hexapeptide Valine-Leucin-Proline-Alanine-Leucine-Proline (VLPALP) was designed, which demonstrated it to have the same protective effects as the 400-2000 Da NMPF fraction. These results indicate a new strategy for the treatment of septic shock and the potential of therapeutic use of this synthetic oligopeptide.

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2002 ACS
AN 1998:629141 CAPLUS
DN 130:90829
TI Effect of human chorionic gonadotropin on T cell phenotypic subpopulation and cytokine secreting subset
AU Wang, Yue; Pan, Jufen
CS Department of Immunology, Tianjin Medical University, Tianjin, 300070, Peop. Rep. China
SO Mianyixue Zazhi (1998), 14(3), 165-168, 193
CODEN: MIZAED; ISSN: 1000-8861
PB Mianyixue Zazhi Bianjibu
DT Journal
LA Chinese
AB The effect of **hCG** (human Chorionic Gonadotropin) on different subset of T cells was studied in vitro by using the expressing of CD3, CD4 and CD8 mols. as the parameter of T cell phenotypic subpopulation, and the secretion of IFN .gamma. and IL-4 as the parameter of **Th1** and **Th2** functional subpopulation. The results showed that **hCG** can inhibit either phenotypic or functional T cell subset in a ranged dose. These inhibition effects can be blocked after the effective ranged dose of **hCG** were neutralized by anti-**hCG** .beta. and anti-intact **hCG**. The inhibition effect can not be blocked by anti-**hCG** .alpha. monoclonal antibodies. The .beta.-subunit or intact-**hCG** is the effective epitope on inhibition of T cell phenotypic expression or cytokine secreting function on **hCG** mol.

L7 ANSWER 12 OF 13 MEDLINE DUPLICATE 6
AN 1999111192 MEDLINE
DN 99111192 PubMed ID: 9815634
TI Effects of a beta-human chorionic gonadotropin subunit immunogen administered in aqueous solution with a novel nonionic block copolymer adjuvant in patients with advanced cancer.
AU Triozzi P L; Stevens V C; Aldrich W; Powell J; Todd C W; Newman M J
CS The Ohio State University Comprehensive Cancer Center, 410 West 10th Ave, Columbus, Ohio 43210, USA.
NC 2P30CA26508 (NCI)
SO CLINICAL CANCER RESEARCH, (1997 Dec) 3 (12 Pt 1) 2355-62.
Journal code: 9502500. ISSN: 1078-0432.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199903
ED Entered STN: 19990316
Last Updated on STN: 19990316
Entered Medline: 19990303
AB The clinical and immunological effects of a vaccine consisting of CTP37, a synthetic peptide corresponding to the COOH-terminal peptide (CTP) of beta-human chorionic gonadotropin (beta-**hCG**) conjugated to diphtheria toxoid, combined with CRL 1005, a novel synthetic nonionic block copolymer adjuvant, were examined. Twenty-one patients with metastatic, nontrophoblastic cancers received up to four immunizations by i.m. injection of a fixed dose of CTP37 and escalating doses of CRL 1005. Doses of CRL 1005 adjuvant as high as 75 mg were administered with 1 mg of CTP37 without evidence of significant local or systemic toxicity. Immunizations resulted in the production of IgG antibody to beta-**hCG**. CRL 1005 doses of 3-25 mg appeared to be optimal for antibody induction. Immunizations also resulted in increases in the cellular response of peripheral blood mononuclear cells (PBMCs) to the unconjugated CTP, **hCG**, and diphtheria toxoid. Responding PBMCs specifically secreted the **TH1**-associated cytokines IFN-gamma and interleukin (IL)-2 as well as the **TH2**-associated IL-5 and IL-10. Increased expression of IFN gamma and IL-5 mRNAs by PBMCs 4 h after immunization was

also observed. CRL 1005 administered with CTP37 in aqueous solution is well tolerated. The CTP37-CRL 1005 subunit vaccine has the capacity to stimulate potentially beneficial humoral and cellular immune responses in patients with advanced cancer.